In this personal essay, presented as the keynote address at the inaugural meeting of the Australasian Cleft Palate Association, the author provides an overview of what many might call “the state-of-the-art.” But beyond that, the author also plots direction to our efforts so our science can progress.

KEY WORDS: cleft lip, cleft palate, research, genetics, surgery

ETIOLOGY AND PREVENTION

With the rapid advances that are now being made in molecular biology, it is likely that our knowledge of the etiology of cleft lip and palate will increase greatly over the next decade. The precise location of many loci responsible for the common genetic diseases will be known, and more reliable probing methods will be available for describing the genotype. Genes that cause clefts will be mapped and investigated by recombinant DNA probes, making it possible to identify the carriers of these mutant genes. Increased knowledge of cell biology might eventually lead to the possibility of prevention of clefts of the lip and palate. This will particularly apply in cases with monogenic etiology and in chromosomal disorders. However, the large multifactorial polygenic group will be more elusive. Here clefting is the result of possible defects in a number of genes, acting in conjunction with environmental factors that are as yet unknown.

At present our knowledge of the teratogens that are associated with facial clefting is very limited. Only a few substances such as retinoic acid (used in the treatment of acne and psoriasis), hydantoin, and alcohol have been confirmed as teratogens with direct effects on facial morphogenesis. Obviously, others await identification.

Metabolic disorders that may or may not be inherited could be predisposing factors in clefting. The midline is an area of developmental instability in the embryo. An inability to metabolize folic acid is present in some cases of spina bifida. Metabolic disorders therefore also present another avenue for investigation.

Monozygous twins discordant for clefting are intriguing. Is the etiology of these clefts multifactorial with polygenic influences present in both twins? Has an environmental factor acted on one twin alone? There is another possible explanation: Examinations of the developing fetus by ultrasound have shown that there are altered rates of fetal growth, both of the whole body and of its parts, so that at any one time twins may exhibit different stages of development. Therefore, the variable expression of clefting could result from the same factor acting on both twins at the same time, but at relatively different stages of their early growth. Of course, the factor could be genetic, teratogenic, or a metabolic defect.

At present, the prevention of most clefts is not possible without knowing the precise etiology. Genetic counseling can identify high risk patients, and ultrasound at 18 weeks gestation can reveal markers of syndromes associated with clefts. The clefts themselves may be visible at 20 weeks. But beyond early identification, we can only look to the future.

TIMING OF REPAIR

To date, there has been no generally agreed timetable for repair of clefts of the lip and palate. Until recently the timing of surgical repair has been dictated by the anesthetics of yesteryear. The child had to be 10 pounds in weight and gaining before the lip was repaired. Palate repair was delayed as long as possible. However, the problems of intubation, fluid replacement, and suitable anesthetic agents have now been overcome. Long surgical procedures can be performed safely in the neonatal period, and we can rethink the optimum time for cleft surgery.

Clearly there is much in favor of early repair of the anomaly. Early repair of the palate should allow more normal speech development, and early lip repair might promote better healing of the lip. On the other hand, the effects of early repair on growth have yet to be determined, and there are certainly technical problems in neonatal surgery.

A decision is also required on the correct sequence of repair in regard to the effects of muscle balance and scarring. Does a long delay between lip repair and palate closure create a muscle imbalance that has an effect on skeletal and arch development? If muscle imbalance is problematic, then perhaps complete clefts of the lip and palate should be repaired in a single stage or with as little delay as possible between the lip and palate closures. In Perth we are now moving toward repair of the cleft lip, nose, and hard palate at 6 weeks of age, followed by repair of the soft palate 6 weeks later, so that the repair can be completed by the time the child is 3 months old. Will there be interference with growth by this earlier operation? The repair is certainly
technically more difficult. In balance, will the final result be a gain or loss?

The ability to diagnose facial clefts by ultrasound offers the prospect of prenatal repair of the defect. Intrauterine fetal wounds heal without inflammatory response and with negligible scar formation. Furthermore, muscle fibers actively regenerate and migrate across the wound margin. The risks to both the mother and the fetus will have to be defined carefully. Obviously, subsequent deliveries by caesarian section would be mandatory following hysteroscopy and intrauterine repair.

**Bilateral Cleft Lip and Palate**

Bilateral cleft lip and palate is still poorly understood, and its problems are far from solved. Apart from intrinsic deficiency of tissue, there is difficulty in restoring the orbicularis oris muscle and in creating a philtrum. Will strands of crossing free muscle grafts have a place here in the future to provide dynamic modeling of the lip structure and avoid the flattened inanimate appearance of the center of the lip?

The protruding premaxilla often lies below the level of the occlusal plane. Can this be molded upward by presurgical orthopaedics, or must it await segmental osteotomy at a much later age? The problem of the bilateral cleft lip nose also persists. The prolabium has been conveniently used to supply tissue to lengthen the short columella, but what is the real cause of the columellar shortening? Dissections suggest that the alar cartilages have been pulled apart in the nasal tip and that the columella has been shortened back from the nasal tip toward its base. The crura are incorporated in the broad nasal tip. Is the skin distance across the nasal tip from alar base to alar base greater in infants with bilateral clefts than in normal babies? Baseline records of facial dimensions are necessary before this question and many others can be answered.

Perhaps microsurgery will be used in the dissection and correction of the displaced alar cartilages, to reconstruct the columella. It seems likely that more refined microsurgical techniques will be used in the future for cleft repairs, and these will be based on further anatomic studies.

**Maxillary Arch**

The results of delayed bone grafting of the alveolar cleft have been highly successful in restoring an intact dental arch. However, an otherwise excellent result may be compromised by subsequent tooth displacement that is caused by palatal scarring created by the original palate repair. Having set a normal dental arch as our goal, is it possible to prevent tooth displacement by repairing the palate without significant dissection of flaps from the hard palate?

**Assessment**

With the increasing sophistication of cleft repairs, it is becoming difficult, and even impossible, to compare and evaluate the effectiveness of new methods of treatment. We urgently require stricter criteria for reporting and objective standards for the assessment of our work.

In a recent editorial in *Plastic and Reconstructive Surgery*, Bardach (1987) pointed to the absence of publications devoted to the study of late results of cleft lip and palate treatment. There are in fact virtually no analyses of late results of multidisciplinary treatment. If we are to progress with surgical refinements, we require better clinical research and studies based on *long-term* results. We must have more reliable, complete information on the effectiveness of new and current procedures.

In 1987, Ross reviewed cephalometric radiographs of 539 white males with unilateral clefts of the lip and palate. These came from 15 centers around the world. With this information he was able to describe the basic intrinsic deficiency in the midfacial skeleton in individuals with unilateral clefts of the lip and palate. From a knowledge of treatment regimens, he was then able to identify those procedures, and their timing of application, that seemed to produce maximum or minimum interference with skeletal growth. Unfortunately, his study was incomplete. It investigated neither the transverse dimensions of the facial skeleton nor the form of the alveolar arch and the position of individual teeth. But Ross’s material is the type of basic data that we require and that is long overdue. It is to be hoped that, in the future, international data bases of facial and skeletal norms will be established to set out the basic growth in each type of cleft and for each racial group. These will provide yardsticks against which new treatment procedures can be measured.

In surgery for clefts, we are primarily concerned with restoring a facial appearance as normal as possible. When a new surgical procedure is presented for correction of the lip or nose of a patient with a cleft, it is no longer sufficient to show one or two examples for evaluation. It should be absolutely mandatory to present the results in an average sample. This sample should be a consecutive series of at least 10 patients, not only in the early postoperative period, but also followed through their later growth and preferably with eventual final follow-up photographs after puberty. Statistically significant numbers must be presented. In the future, it may be possible to quantify asymmetry and disfigurement by recording contour lines such as those produced by Moire photography or by new computer techniques. We are all aware that lip repairs that look satisfactory in static photographs can develop muscle bunching and contour irregularities on movement. Videorecording in our later results should become standard in cleft lip and palate clinics, and should be shown more often at our meetings.

Normal speech is a major goal of treatment, but so far there is no generally accepted standardized assessment by which results of treatment can be compared. To report that ‘speech results are very encouraging’ after a new procedure is simply not good enough. Standardized speech assessment should be developed at least on a national basis and preferably internationally. While the ear is the final arbiter, more objective assessment by instrumental measurement of resonance and nasal air emission may be the basis for standardized assessment in the future. Standardized speech assessment will facilitate investigations into the effects of age at the time of palate repair and the types of palate closure and of pharyngoplasty.

Velopharyngeal function and closure patterns deserve further investigation, particularly with reference to the strength and vertical aspect of velopharyngeal closure. De-
development of dynamic magnetic resonance imaging would be a valuable tool.

CONCLUSION

This is a personal view of the horizons of cleft research. Some of these problems may have already been solved. As surgeons who are operating on growing tissues, it is good to be hesitant about rushing to perform the latest published operation. But unless we should be too hesitant, it is also well to remember that much of today’s accepted treatment was probably considered experimental surgery 20 years ago, and in turn it might be regarded as surgical negligence in 20 years time.

REFERENCES